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FILE LAST UPDATED: 7 Dec 2009 (20091207/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

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L1 STR
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OH

Structure attributes must be viewed using STN Express query preparation. L3  $\,$  115 SEA FILE=REGISTRY SSS FUL L1  $\,$ 

L4 10 SEA FILE=CAPLUS L3

## => d 14 1-10 ibib abs hitstr

L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:855540 CAPLUS

DOCUMENT NUMBER: 151:173252

TITLE: Preparation of 2- and 3-substituted

5,6-diarylpyridines as CB1 cannabinoid receptor

antagonists

INVENTOR(S): Barre, Lionel; Congy, Christian; Pointeau, Philippe;

Rinaldi-Carmona, Murielle

PATENT ASSIGNEE(S): Sanofi-Aventis, Fr. SOURCE: PCT Int. Appl., 81pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French FAMILY ACC. NUM. COUNT: 2

PARENT THEODMANTON

PATENT INFORMATION:

	PATENT NO.					KIND DATE				APPLICATION NO.						DATE			
	WO 2009087285								WO 2008-FR1421				20081010						
	W:	ΑE,	AG,	AL,	AM,	AO,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,		
		CA,	CH,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DO,	DZ,	EC,	EE,	EG,	ES,		
		FI,	GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,		
		KG,	KM,	KN,	KP,	KR,	KΖ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,		
		ME,	MG,	MK,	MN,	MW,	MX,	MY,	MΖ,	NA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,		
		PL,	PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	ST,	SV,	SY,	ТJ,		
		TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	ZW				
	RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	HR,	HU,		
		ΙE,	IS,	IT,	LT,	LU,	LV,	MC,	MT,	ΝL,	NO,	PL,	PT,	RO,	SE,	SI,	SK,		
		TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,		
		ΤG,	BW,	GH,	GM,	KE,	LS,	MW,	MΖ,	NΑ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,		
		AM,	ΑZ,	BY,	KG,	KΖ,	MD,	RU,	ΤJ,	TM									
FR	FR 2922209				A1		2009	0417		FR 2	007-	7186			2	20071012			
PRIORITY	PRIORITY APPLN. INFO.:									FR 2	007-	7186			A 20071012				
OTHER SO	OTHER SOURCE(S):				MAR:	PAT	151:	1732	52										
GI																			

II

AB Title compds. I [Q = O, S, NR1; R1 = H, alkyl; Z = NR3XR4, NR3COOR5, OCONR3R5; X = CO, SO2, CONR6, CSNR6; R3, R6 = independently H, alkyl; R4 = (un) substituted alkyl, Ph, indolyl, etc.; R5 = (un) substituted phenyl; Ar1, Ar2 = independently (un) substituted phenyl; Y = CN, (un) substituted phenoxy, alkoxycarbonyl, alkylsulfonyl, CONH2 and derivs., etc.; A = (CH2)n; n = 0-1; B = (Alk')m; Alk' = linear or branched C1-5 alkyl; m = 10-1; their free bases and their addition salts were prepared as antagonists of CB1 cannabinoid receptors (no data) and for treatment of the diseases it implies (no data). Thus, a multi-step synthesis starting from [6-(4-bromopheny1)-5-(2,4-dichloropheny1)-2-(methoxymethy1)pyridin-3yl]methanol was given for diphenylpyridine II. I exhibited an excellent affinity in vitro (IC50  $\leq$  5 $\bullet$ 10-7 M) for the CB1 cannabinoid receptors. The antagonist nature of compds. I was demonstrated by adenylate-cyclase inhibition models, and toxicity was compatible with therapeutic use (no data). The interaction of I with the brain CB1 receptors was determined using a test of ex vivo binding of [3H]-CP55940 after i.v. injection to mice (no data). The interaction of I with the peripheral CB1 receptors was determined using a test of reversion of the inhibiting effect of CP55940 on gastrointestinal transit after oral administration to mice (no data). Thus, I are useful for treating psychiatric, metabolic, and gastrointestinal disorders, drug dependence, etc. (no data).

IT 1173144-25-6P, N-[[6-(4-Chlorophenyl)-5-(2,4-dichlorophenyl)-3 [[(2-fluorobenzyl)carbamoyl]amino]methyl]pyridin-2-yl]methyl]-2 hydroxyacetamide 1173144-28-9P,
 N-[[6-(4-Chlorophenyl)-5-(2,4-dichlorophenyl)-2 [[(hydroxyacetyl)amino]methyl]pyridin-3-yl]methyl]-4 (trifluoromethyl)benzamide
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); RACT (Reactant or reagent); USES (Uses)
 (drug candidate; preparation of diphenylpyridines as antagonists of CB1

RN 1173144-25-6 CAPLUS

cannabinoid receptors)

CN Acetamide, N-[[6-(4-chloropheny1)-5-(2,4-dichloropheny1)-3-[[[[(2-fluoropheny1)methy1]amino]carbony1]amino]methy1]-2-pyridiny1]methy1]-2-hydroxy- (CA INDEX NAME)

RN 1173144-28-9 CAPLUS

CN Benzamide, N-[[6-(4-chloropheny1)-5-(2,4-dichloropheny1)-2-[[(2-hydroxyacety1)amino]methy1]-3-pyridiny1]methy1]-4-(trifluoromethy1)- (CA INDEX NAME)

IT 1143624-05-8P 1143625-17-5P, N-[[6-(4-Bromophenyl)-5-(2,4-dichlorophenyl)-2-[[(hydroxyacetyl)amino]methyl]pyridin-3-yl]methyl]-4-[(trifluoromethyl)thio]benzamide 1173144-12-1P 1173144-13-2P 1173144-14-3P 1173144-31-4P, N-[[6-(4-Chlorophenyl)-5-(2,4-dichlorophenyl)-2-[[(hydroxyacetyl)amino]methyl]pyridin-3-yl]methyl]-4-[(trifluoromethyl)thio]benzamide RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (drug candidate; preparation of diphenylpyridines as antagonists of CB1 cannabinoid receptors) RN 1143624-05-8 CAPLUS Benzamide, N-[[6-(4-bromopheny1)-5-(2,4-dichloropheny1)-2-[[(2-bromopheny1)-2-(2,4-dichloropheny1)-2-(3,4-dichloropheny1)-2-(3,4-dichloropheny1)-2-(3,4-dichloropheny1)-2-(3,4-dichloropheny1)-3-(3,4-dichloCN

hydroxyacetyl)amino]methyl]-3-pyridinyl]methyl]-4-[(trifluoromethyl)thio]-

F3C-S

O

CH2-NH-C-CH2-OH

Br

C1

C1

, hydrochloride (1:1) (CA INDEX NAME)

## ● HCl

RN 1143625-17-5 CAPLUS

CN Benzamide, N-[[6-(4-bromopheny1)-5-(2,4-dichloropheny1)-2-[[(2-hydroxyacety1)amino]methy1]-3-pyridiny1]methy1]-4-[(trifluoromethy1)thio]-(CA INDEX NAME)

RN 1173144-12-1 CAPLUS

CN Benzamide, N-[[6-(4-chlorophenyl)-5-(2,4-dichlorophenyl)-2-[[(2-hydroxyacetyl)amino]methyl]-3-pyridinyl]methyl]-4-[(trifluoromethyl)thio]-, hydrochloride (1:1) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ & \\ & & \\$$

● HCl

RN 1173144-13-2 CAPLUS

CN Acetamide, N-[[6-(4-chlorophenyl)-5-(2,4-dichlorophenyl)-3-[[[[(2-fluorophenyl)methyl]amino]carbonyl]amino]methyl]-2-pyridinyl]methyl]-2-hydroxy-, hydrochloride (1:1) (CA INDEX NAME)

● HCl

RN

 $1173144-14-3 \quad \text{CAPLUS} \\ \text{Benzamide, N-[[6-(4-chlorophenyl)-5-(2,4-dichlorophenyl)-2-[[(2-dichlorophenyl)-2-[$ CN hydroxyacetyl)amino]methyl]-3-pyridinyl]methyl]-4-(trifluoromethyl)-, hydrochloride (1:1) (CA INDEX NAME)

F3C 
$$CH_2-NH-C-CH_2-OH$$
  $C1$   $C1$ 

● HCl

1173144-31-4 CAPLUS RN

Benzamide, N-[[6-(4-chlorophenyl)-5-(2,4-dichlorophenyl)-2-[[(2-dichlorophenyl)-2-[(3-dichlorophenyl)-2-(3-dichlorophenyl)-2-(3-dichlorophenyl)-2-[(3-dichlorophenyl)-3-(3-dichCN hydroxyacetyl)amino]methyl]-3-pyridinyl]methyl]-4-[(trifluoromethyl)thio]-(CA INDEX NAME)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:457259 CAPLUS

DOCUMENT NUMBER: 150:447705

TITLE: Preparation of 2- and 3-substituted

5,6-diarylpyridines as CB1 cannabinoid receptor

antagonists

INVENTOR(S): Barre, Lionel; Congy, Christian; Pointeau, Philippe;

Rinaldi, Carmona Murielle

PATENT ASSIGNEE(S): Sanofi Aventis, Fr. SOURCE: Fr. Demande, 66pp.

CODEN: FRXXBL

DOCUMENT TYPE: Patent LANGUAGE: French

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

GΙ

PA:	PATENT NO.					KIND DATE			APPLICATION NO.						DATE			
FR	2922209				A1	_	20090417		FR 2007-7186						20071012			
WO	2009	0872	85		Α1		20090716			WO 2008-FR1421					20081010			
	W:	ΑE,	AG,	AL,	ΑM,	ΑO,	ΑT,	ΑU,	ΑZ,	ΒA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,	
		CA,	CH,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DO,	DZ,	EC,	EE,	EG,	ES,	
		FI,	GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	ΙL,	IN,	IS,	JΡ,	KE,	
		KG,	KM,	KN,	KP,	KR,	ΚZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,	
		ME,	MG,	MK,	MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,	
		PL,	PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	ST,	SV,	SY,	TJ,	
		TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	ZW			
	RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HR,	HU,	
		ΙE,	IS,	IT,	LT,	LU,	LV,	MC,	MT,	NL,	NO,	PL,	PT,	RO,	SE,	SI,	SK,	
		TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	
		TG,	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	
		AM,	AZ,	BY,	KG,	KΖ,	MD,	RU,	ΤJ,	TM								
PRIORIT	PRIORITY APPLN. INFO.:									FR 2007-7186					A 20071012			
OTHER SO	OTHER SOURCE(S):				MARPAT 150:447705													

AB Title compds. I [Q = 0, S, NR1; R1 = H, alkyl; Z = NR3XR4, NR3COOR5, OCONR3R5; X = CO, SO2, CONR6, CSNR6; R3, R6 = independently H, alkyl; R4 = (un)substituted alkyl, Ph, indolyl, etc.; R5 = (un)substituted phenyl; Ar1, Ar2 = independently (un)substituted phenyl; Y = CN, (un)substituted phenoxy, alkoxycarbonyl, alkylsulfonyl, CONH2 and derivs., etc.; A = (CH2)n; n = 0-1; B = (Alk')m; Alk' = linear or branched C1-5 alkyl; m = 0-1; their free bases and their addition salts, and their hydrates and solvates] were prepared as antagonists of CB1 cannabinoid receptors (no data) and for treatment of the diseases it implies (no data). Thus, a multi-step synthesis starting from [6-(4-bromophenyl)-5-(2,4-dichlorophenyl)-2-(methoxymethyl)pyridin-3-

ΙI

yl]methanol was given for diphenylpyridine II. I exhibited an excellent affinity in vitro (IC50  $\leq$  5•10-7 M) for the CB1 cannabinoid receptors. The antagonist nature of compds. I was demonstrated by adenylate-cyclase inhibition models, and toxicity was compatible with therapeutic use (no data). The interaction of I with the brain CB1 receptors was determined using a test of ex vivo binding of [3H]-CP55940 after i.v. injection to mice (no data). The interaction of I with the peripheral CB1 receptors was determined using a test of reversion of the inhibiting effect of CP55940 on gastrointestinal transit after oral administration to mice (no data). Thus, I are useful for treating psychiatric, metabolic, and gastrointestinal disorders, smoking cessation, etc. (no data).

IT 1143624-05-8P 1143625-17-5P,

N-[[6-(4-Bromopheny1)-5-(2,4-dichloropheny1)-2-[(2-hydroxyacetylamino)methyl]pyridin-3-yl]methyl]-4-

[(trifluoromethyl)thio]benzamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of diphenylpyridines as antagonists of CB1 cannabinoid receptors)  $\,$ 

RN 1143624-05-8 CAPLUS

CN Benzamide, N-[[6-(4-bromopheny1)-5-(2,4-dichloropheny1)-2-[[(2-hydroxyacety1)amino]methy1]-3-pyridiny1]methy1]-4-[(trifluoromethy1)thio]-, hydrochloride (1:1) (CA INDEX NAME)

● HCl

RN 1143625-17-5 CAPLUS

CN Benzamide, N-[[6-(4-bromophenyl)-5-(2,4-dichlorophenyl)-2-[[(2-hydroxyacetyl)amino]methyl]-3-pyridinyl]methyl]-4-[(trifluoromethyl)thio]-(CA INDEX NAME)

F3C-S 
$$CH_2-NH-C-CH_2-OH$$
  $Br$   $C1$ 

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:276997 CAPLUS

DOCUMENT NUMBER: 150:447822

TITLE: Process Development of a Potent Bradykinin 1

Antagonist

AUTHOR(S): Menzel, Karsten; Machrouhi, Fouzia; Bodenstein,

Matthew; Alorati, Anthony; Cowden, Cameron; Gibson, Andrew W.; Bishop, Brian; Ikemoto, Norihiro; Nelson,

Todd D.; Kress, Michael H.; Frantz, Doug E.

CORPORATE SOURCE: Merck Research Laboratories, Department of Process

Research, Merck and Co. Inc., Wayne, PA, 19087, USA

SOURCE: Organic Process Research & Development (2009), 13(3),

519-524

Ι

CODEN: OPRDFK; ISSN: 1083-6160

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

GΙ

AΒ As part of Merck's continued research effort on inflammation and pain, a safe synthesis of an orally bioavailable and CNS penetrant bradykinin 1 antagonist was developed and demonstrated on kilogram scale. The key step included a novel regioselective metal-halogen exchange reaction on 1,2-dibromo-5-chloro-3-fluorobenzene using isopropylmagnesium chloride to install the 1,2,4-oxadiazole ring structure. Suzuki cross-coupling reaction between a highly functionalized and sterically hindered electrophile and boronic ester generated the biaryl ring system, which was converted to the target mol. (I) using standard chemical The safe installation of a 1,2,4-oxadiazole ring proved to be challenging since the original synthetic route relied on the preparation of a highly functionalized benzonitrile using potassium cyanide and resulted in low yields and large amts. of potentially hazardous waste. Overall, a safe and robust synthesis was developed, which occurred in eight linear steps with an overall yield of 28%.

IT 858412-39-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of a Bradykinin 1 antagonist in a safe and robust manner over eight linear steps)

RN 858412-39-2 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[5-chloro-3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:1472960 CAPLUS

DOCUMENT NUMBER: 150:159291

TITLE: Fractional mass filtering as a means to assess

circulating metabolites in early human clinical

studies

AUTHOR(S): Tiller, Philip R.; Yu, Sean; Bateman, Kevin P.;

Castro-Perez, Jose; McIntosh, Ian S.; Kuo, Yushin;

Baillie, Thomas A.

CORPORATE SOURCE: Merck Research Laboratories, West Point, PA, 19486,

USA

SOURCE: Rapid Communications in Mass Spectrometry (2008),

22(22), 3510-3516

CODEN: RCMSEF; ISSN: 0951-4198

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

AΒ Recent changes in the regulatory environment have led to a need for new methods to assess circulating human drug metabolites in early clin. studies with respect to their potential toxicol. impact. The specific goals of such studies are to determine if the metabolites present in human plasma following administration of a drug candidate also are observed in plasma from the animal studies employed for preclin. toxicol. evaluation, and to estimate corresponding exposure margins (animal:human) for the major metabolites. Until recently, the accepted best practice for the characterization of circulating drug metabolites utilized liquid  ${\tt chromatog./tandem\ mass\ spectrometry\ (LC/MS/MS)-based\ methodologies,\ in}$ conjunction with authentic chemical stds., for the detection and quant. analyses of metabolites predicted from both animal studies and expts. with human liver prepns. in vitro. While this approach is satisfactory for anticipated biotransformation products, metabolites that were not expected to circulate in human plasma frequently escape detection. Current accurate mass instruments enable the use of the technique of fractional mass filtering to detect both expected and unexpected metabolites in a rapid, less resource-intensive and more robust manner. Application of this technol. to several clin. development programs at Merck Research Labs. has demonstrated the value of fractional mass filtering in the assessment of circulating drug metabolites in early clin. trials.

IT 858412-39-2

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

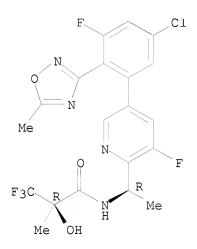
(drug candidate; fractional mass filtering as a means to assess

circulating metabolites in early human clin. studies)

RN 858412-39-2 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[5-chloro-3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD

(7 CITINGS)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:1136067 CAPLUS

DOCUMENT NUMBER: 149:534142

TITLE: Bradykinin B1 receptor antagonists: An  $\alpha$ -hydroxy

amide with an improved metabolism profile

AUTHOR(S): Kuduk, Scott D.; Chang, Ronald K.; DiPardo, Robert M.;

Di Marco, Christina N.; Murphy, Kathy L.; Ransom,

Richard W.; Reiss, Duane R.; Tang, Cuyue;

Prueksaritanont, Thomayant; Pettibone, Douglas J.;

Bock, Mark G.

CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research

Laboratories, West Point, PA, 19486, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2008),

18(18), 5107-5110

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 149:534142

GI

10/583,675

AB A series of carbo- and heterocyclic  $\alpha$ -hydroxy amide-derived bradykinin B1 antagonists, e.g., I, was prepared and evaluated. A 4,4-difluorocyclohexyl  $\alpha$ -hydroxy amide was incorporated along with a 2-Me tetrazole in lieu of an oxadiazole to afford a suitable compound with good pharmacokinetic properties, CNS penetration, and clearance by multiple metabolic pathways.

IT 858412-39-2

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)

(preparation, bradykinin B1 receptor binding affinities, P-glycoprotein transport properties, and pharmacokinetics of  $\alpha$ -hydroxy amides incorporating a Me tetrazole substituent)

RN 858412-39-2 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[5-chloro-3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:85173 CAPLUS

DOCUMENT NUMBER: 148:369250

TITLE:  $\alpha$ -Hydroxy amides as a novel class of bradykinin

B1 selective antagonists

AUTHOR(S): Wood, Michael R.; Schirripa, Kathy M.; Kim, June J.;

Kuduk, Scott D.; Chang, Ronald K.; Di Marco, Christina
N.; DiPardo, Robert M.; Wan, Bang-Lin; Murphy, Kathy
L.; Ransom, Richard W.; Chang, Raymond S. L.; Holahan,
Marie A.; Cook, Jacquelynn J.; Lemaire, Wei; Mosser,

Scott D.; Bednar, Rodney A.; Tang, Cuyue;

Prueksaritanont, Thomayant; Wallace, Audrey A.; Mei, Qin; Yu, Jian; Bohn, Dennis L.; Clayton, Frank C.; Adarayn, Emily D.; Sitko, Gary R.; Leonard, Yvonne M.; Freidinger, Poger M.; Pettibore, Douglas J.; Book

Freidinger, Roger M.; Pettibone, Douglas J.; Bock,

Mark G.

CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research

Laboratories, West Point, PA, 19486, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2008),

18(2), 716-720

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

AB Antagonism of the bradykinin B1 receptor represents a potential treatment for chronic pain and inflammation. Novel antagonists incorporating  $\alpha\text{-hydroxy}$  amides were designed that display low-nanomolar affinity for the human bradykinin B1 receptor and good bioavailability in the rat

and dog. In addition, these functionally active compds. show high passive permeability and low susceptibility to phosphoglycoprotein mediated efflux, predictive of good CNS exposure.

IT 858412-39-2 858412-99-4 858413-47-5

858413-50-0 858413-57-7 858413-64-6 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

 $(\alpha-hydroxy amides as bradykinin B1 antagonists)$ 

RN 858412-39-2 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[5-chloro-3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-

, (2R) - (CA INDEX NAME)

RN 858412-99-4 CAPLUS

CN Benzoic acid, 2,4-dichloro-6-[5-fluoro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-47-5 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[5-chloro-3-fluoro-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

RN

CN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-57-7 CAPLUS RN

CNPropanamide, N-[(1R)-1-[3-chloro-5-[5-chloro-3-fluoro-2-(2-methyl-2H-fluoro-2-(2-methytetrazol-5-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2methyl-, (2R)- (CA INDEX NAME)

RN 858413-64-6 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3,5-dichloro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD

(6 CITINGS)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:793702 CAPLUS

DOCUMENT NUMBER: 147:166197

TITLE: Preparation of tartaric acid functional compounds for

the treatment of disorders mediated by MMPs, aggrecanase, ADMP, LpxC, ADAMs, TACE and  $\text{TNF-}\alpha$ 

INVENTOR(S): Siddiqui, M. Arshad; Mansoor, Umar Faruk; Reddy,

Panduranga Adulla P.; Madison, Vincent S.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: U.S. Pat. Appl. Publ., 556pp., Cont.-in-part of U.S.

Ser. No. 291,595.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070167426	A1	20070719	US 2006-599784	20061115
US 20060252778	A1	20061109	US 2005-142601	20050601
US 20060178366	A1	20060810	US 2005-291595	20051201
PRIORITY APPLN. INFO.:			US 2004-576153P P	20040602
			US 2005-142601 A	2 20050601
			US 2005-291595 A	2 20051201

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 147:166197

GΙ

The title compds. I [A = (un)substituted benzimidazol-2-yl, imidazol-2-yl, CONH2, CSNH2, etc.; J, E = O, S, NR5 (wherein R5 = H, alkyl, alkylaryl); T = O, S; R10, R20 = H, alkyl, fluoroalkyl; R30 = H, alkyl or R30 and R40, taken together with N to which R40 is attached, are joined to form 4-7 membered (un)substituted heterocyclyl; R40, R50 = H, alkyl; W = [C(R13)2]n (wherein n = 0-5 or a bond; R13 = H, halo, OH, etc.); X = a bond, alkyl, cycloalkyl, etc.; Y = a bond, O, S, NH, etc.; Z = H, alkyl, aryl, etc.; or their pharmaceutically acceptable salts] which can be useful for the treatment of diseases or conditions mediated by MMPs, aggrecanase, ADMP, LpxC, ADAMs, TACE and TNF- $\alpha$ , were prepared E.g., a multi-step synthesis of II, starting from 2,2-dimethyl-[1,3]dioxolane-4R,5R-dicarboxylic acid monomethyl ester and 2-(thien-1-yl)ethylamine, was given. The compds. I were tested against LpxC and ADMP (biol. data given for representative compds. I).

IT 871713-82-5P 871713-83-6P 871713-84-7P 871713-85-8P 871713-88-1P 871713-89-2P

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871713-90-5P
                       871713-91-6P
                                         871713-92-7P
     871713-93-8P
                       871713-94-9P
                                         871713-95-0P
     871713-96-1P
                       871723-96-5P
                                         871723-99-8P
                       871724-05-9P
                                         871728-75-5P
     871724-02-6P
     871728-76-6P
                       871728-77-7P
                                         871728-78-8P
     871728-79-9P
                       871728-80-2P
                                         871729-25-8P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of tartaric acid functional compds. for treating inflammation,
        microbial infection, and other disorders mediated by MMPs, aggrecanase,
        ADMP, LpxC, ADAMs, TACE and TNF-\alpha)
     871713-82-5 CAPLUS
RN
CN
     1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-chlorophenyl)-2-
     pyridinyl]methyl]-\alpha, \beta-dihydroxy-\gamma-oxo-,
     (\alpha R, \beta R) - (CA INDEX NAME)
```

Absolute stereochemistry.

RN 871713-83-6 CAPLUS CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[(5-phenyl-2-pyridinyl)methyl]-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-84-7 CAPLUS CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-(2-methoxyphenyl)-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

RN 871713-85-8 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-88-1 CAPLUS

CN 2H-Isoindole-2-butanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]-1,3-dihydro- $\alpha$ , $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-89-2 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

RN 871713-90-5 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]-  $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-2-(2-thiazolyl)-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-91-6 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]-2-(4-fluorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-92-7 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-ethoxyphenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

RN 871713-93-8 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-[2-(1-methylethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-94-9 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[[5-[2-(phenylmethoxy)phenyl]-2-pyridinyl]methyl]-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-95-0 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-cyanopheny1)-2-pyridiny1]methyl]-  $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

RN 871713-96-1 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-(2-methoxyphenyl)-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)-(CA INDEX NAME)

Absolute stereochemistry.

RN 871723-96-5 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[1-[5-(2-cyanophenyl)-2-pyridinyl]ethyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871723-99-8 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[1-[5-[2-(aminocarbonyl)phenyl]-2-pyridinyl]ethyl]-2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

RN 871724-02-6 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[1-[5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]ethyl]-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871724-05-9 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[1-[5-(2-ethoxyphenyl)-2-pyridinyl]ethyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-75-5 CAPLUS

CN 2H-Isoindole-2-butanamide, N-[[6-cyano-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]-1,3-dihydro- $\alpha$ , $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

RN 871728-76-6 CAPLUS

CN 1-Pyrrolidinebutanamide,  $\alpha$ ,  $\beta$ -dihydroxy-N-[[6-methoxy-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-77-7 CAPLUS

CN 1-Pyrrolidinebutanamide,  $\alpha$ ,  $\beta$ -dihydroxy-N-[[1-oxido-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-78-8 CAPLUS

CN 2H-Isoindole-2-butanamide, 1,3-dihydro- $\alpha$ , $\beta$ -dihydroxy-N-[[1-oxido-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

RN 871728-79-9 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-ethoxy-4-fluoropheny1)-2-pyridiny1]methy1]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-80-2 CAPLUS

CN 1-Pyrrolidinebutanamide,  $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[[5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]-,  $(\alpha R, \beta R)$ - (CA INDEX NAME)

Absolute stereochemistry.

RN 871729-25-8 CAPLUS

CN 2-Pyridinepropanamide,  $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]-,  $(\alpha R, \beta S)$ - (CA INDEX NAME)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:796760 CAPLUS

DOCUMENT NUMBER: 145:230531

TITLE: Preparation of tartaric acid functional compounds for

the treatment of inflammatory disorders mediated by

MMPs, aggrecanase, ADMP, LpxC, ADAMs, TACE and

 $TNF-\alpha$ 

INVENTOR(S): Siddiqui, M. Arshad; Mansoor, Umar Faruk; Reddy,

Panduranga A.; Madison, Vincent S.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 523 pp., Cont.-in-part of U.S.

Ser. No. 142,601.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.				KIND DATE				APPLICATION NO.						DATE			
				A1 A1		2006	US 2005-291595						20051201				
						20061109			US 2005-142601						20050601		
US	2007				A1				US 2006-599784 AU 2006-320621								
AU	2006				A1				-								
	2632					20070607						2632					
WO	2007				A1		2007			WO 2006-US45773 BA, BB, BG, BR, BW, BY,							
	W:																
			,			,		DK,	,	•				,			,
								HU,									
		•			•			LR,		•	•						
		MN,	MW,	MX,	MY,	ΜZ,	NΑ,	NG,	NΙ,	NO,	ΝŹ,	OM,	PG,	PH,	PL,	PT,	RO,
		RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	ТJ,	TM,	TN,	TR,	TT,
								VN,									
	RW:	ΑT,	BE,	ВG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	HU,	IE,
		IS,	ΙΤ,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	BJ,
		CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	ΤG,	BW,	GH,
		GM,	ΚE,	LS,	MW,	ΜZ,	NΑ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	ΚZ,	MD,	RU,	ΤJ,	TM										
EΡ	1957	058			Α1		2008	0820		EP 2	006-	8446	52		20061129		
	R:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,
		IS,	IT,	LI,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	AL,
		BA,	HR,	MK,	RS	·	·	·	·								
JP	2009	5182	94	·	T		2009	0507		JP 2	-800	5434	39		20061129		
MX	2008	0070	92		А		2008	0814	]	MX 2	-800	7092			20080602		

KR 2008071200	A	20080801	KR	2008-715687		20080627
CN 101426486	A	20090506	CN	2006-80052101		20080730
PRIORITY APPLN. INFO.:			US	2004-576153P	P	20040602
			US	2005-142601	A2	20050601
			US	2005-291595	A2	20051201
			WO	2006-US45773	W	20061129

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): MARPAT 145:230531
GI

Ι

AB The title compds. I [A = (un)substituted benzimidazol-2-yl, imidazol-2-yl, CONH2, CSNH2, etc.; J, E = 0, S, NR5 (wherein R5 = H, alkyl, alkylaryl); T = 0, S; R10, R20 = H, alkyl, fluoroalkyl; R30 = H, alkyl or R30 and R40, taken together with N to which R40 is attached, are joined to form 4-7 membered (un)substituted heterocyclyl; R40, R50 = H, alkyl; W = [C(R13)2]n (wherein n = 0-5 or a bond; R13 = H, halo, OH, etc.); X = a bond, alkyl, cycloalkyl, etc.; Y = a bond, O, S, NH, etc.; Z = H, alkyl, aryl, etc.; or their pharmaceutically acceptable salts] which can be useful for the treatment of diseases or conditions mediated by MMPs, aggrecanase, ADMP, LpxC, ADAMs, TACE and TNF- $\alpha$ , were prepared E.g., a multi-step synthesis of II, starting from 2,2-dimethyl-[1,3]dioxolane-4R,5R-dicarboxylic acid monomethyl ester and 2-(thien-1-yl)ethylamine, was given. The compds. I were tested against LpxC and ADMP (biol. data given for representative compds. I).

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(preparation of tartaric acid functional compds. for treating inflammatory disorders mediated by MMPs, aggrecanase, ADMP, LpxC, ADAMs, TACE and  $\text{TNF}-\alpha$ )

RN 871713-82-5 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-chlorophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-83-6 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[(5-phenyl-2-pyridinyl)methyl]-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-84-7 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-(2-methoxyphenyl)-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)-(CA INDEX NAME)

RN 871713-85-8 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-88-1 CAPLUS

CN 2H-Isoindole-2-butanamide, N-[[5-(2-cyanopheny1)-2-pyridiny1]methy1]-1,3-dihydro- $\alpha$ , $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-89-2 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-90-5 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-2-(2-thiazolyl)-,

$$(\alpha R, \beta R, 2R)$$
 - (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-91-6 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]-2-(4-fluorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-92-7 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-ethoxyphenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-93-8 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-[2-(1-methylethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

RN 871713-94-9 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[[5-[2-(phenylmethoxy)phenyl]-2-pyridinyl]methyl]-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-95-0 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]-  $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-96-1 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-(2-methoxyphenyl)-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)-(CA INDEX NAME)

RN 871723-96-5 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[1-[5-(2-cyanophenyl)-2-pyridinyl]ethyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871723-99-8 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[1-[5-[2-(aminocarbonyl)phenyl]-2-pyridinyl]ethyl]-2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871724-02-6 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[1-[5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]ethyl]-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

RN 871724-05-9 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[1-[5-(2-ethoxyphenyl)-2-pyridinyl]ethyl]- $\alpha$ , $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-75-5 CAPLUS

CN 2H-Isoindole-2-butanamide, N-[[6-cyano-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]-1,3-dihydro- $\alpha$ , $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-76-6 CAPLUS

CN 1-Pyrrolidinebutanamide,  $\alpha$ ,  $\beta$ -dihydroxy-N-[[6-methoxy-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

RN 871728-77-7 CAPLUS

CN 1-Pyrrolidinebutanamide,  $\alpha$ ,  $\beta$ -dihydroxy-N-[[1-oxido-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-78-8 CAPLUS

CN 2H-Isoindole-2-butanamide, 1,3-dihydro- $\alpha$ , $\beta$ -dihydroxy-N-[[1-oxido-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-79-9 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-ethoxy-4-fluorophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

RN 871728-80-2 CAPLUS

CN 1-Pyrrolidinebutanamide,  $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[[5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]-,  $(\alpha R, \beta R)$ - (CA INDEX NAME)

Absolute stereochemistry.

RN 871729-25-8 CAPLUS

CN 2-Pyridinepropanamide,  $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]-,  $(\alpha R, \beta S)$ - (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1331127 CAPLUS

DOCUMENT NUMBER: 144:69727

TITLE: Preparation of tartaric acid functional compounds for

the treatment of inflammatory disorders

INVENTOR(S): Guo, Zhuyan; Orth, Peter; Zhu, Zhaoning; Mazzola,

Robert D.; Chan, Tin Yau; Vaccaro, Henry A.; McKittrick, Brian; Kozlowski, Joseph A.; Lavey, Brian J.; Zhou, Guowei; Paliwal, Sunil; Wong, Shing-Chun; Shih, Neng-Yang; Ting, Pauline C.; Rosner, Kristin E.; Shipps, Gerald W., Jr.; Siddiqui, M. Arshad; Belanger, David B.; Dai, Chaoyang; Li, Dansu; Girijavallabhan, Vinay M.; Popovici-Muller, Janeta; Yu, Wensheng; Zhao,

Schering Corporation, USA PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 889 pp.

CODEN: PIXXD2

Patent DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAI	PATENT NO.								APPLICATION NO.							]	DATE		
	2005		A2				WO 2005-US19131							20050601					
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	ΒA,	BE	3,	BG,	BR,	BW,	BY,	BZ	, CA,	CH,	
																	, GB,		
		GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS	3,	JP,	KΕ,	KG,	KM,	ΚP	, KR,	KΖ,	
		•	•	•	•	•	•	•	•		•	•	•		•		, MZ,	•	
		NG,	ΝI,	NO,	NΖ,	OM,	PG,	PH,	PL,	PI	Γ,	RO,	RU,	SC,	SD,	SE	, SG,	SK,	
		SL,	SM,	SY,	ΤJ,	TM,	TN,	TR,	TT,	TZ	ζ,	UA,	UG,	US,	UΖ,	VC	, VN,	YU,	
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									CA 2005-2569111										
EP									EP 2005-759261 DK, EE, ES, FI, FR,										
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	ORITY APPLN. INFO.:							US 2004-576153P											
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HER SO	IER SOURCE(S):						WO 2005-US19131 W 20050601 CASREACT 144:69727; MARPAT 144:69727												

GΙ

The title compds. I [A = (un)substituted benzimidazol-2-yl, imidazol-2-yl, CONH2, CSNH2; J, E = 0, S, NR5 (wherein R5 = H, alkyl, alkylaryl); T = 0, S; R10, R20 = H, alkyl, fluoroalkyl; R30 = H, alkyl or R30 and R40, taken together with N to which R40 is attached, are joined to form 4-7 membered (un)substituted heterocyclyl; R40, R50 = H, alkyl; W = [C(R13)2]n (wherein n = 0-5; R13 = H, halo, OH, etc.); X = a bond, alkyl, cycloalkyl, etc.; Y = a bond, O, S, NH, etc.; Z = H, alkyl, aryl, etc.; or their pharmaceutically acceptable salts] which can be useful for the treatment of diseases or conditions mediated by MMPs, ADAMs, TACE, TNF- $\alpha$  or combinations thereof, were prepared E.g., a multi-step synthesis of II, starting from 2,2-dimethyl-[1,3]dioxolane-4R,5R-dicarboxylic acid monomethyl ester and 2-(thien-1-yl)ethylamine, was given. The compds. I were tested against TACE (biol. data given for representative compds. I).

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ΙT
     871713-82-5P
                      871713-83-6P
                                        871713-84-7P
     871713-85-8P
                      871713-88-1P
                                        871713-89-2P
     871713-90-5P
                      871713-91-6P
                                        871713-92-7P
     871713-93-8P
                      871713-94-9P
                                        871713-95-0P
     871713-96-1P
                      871723-96-5P
                                        871723-99-8P
     871724-02-6P
                      871724-05-9P
                                        871728-75-5P
     871728-76-6P
                      871728-77-7P
                                        871728-78-8P
                      871728-80-2P
     871728-79-9P
                                        871729-25-8P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of tartaric acid functional compds. for the treatment of inflammatory disorders)

RN 871713-82-5 CAPLUS

1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-chlorophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

RN 871713-83-6 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[(5-phenyl-2-pyridinyl)methyl]-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-84-7 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-(2-methoxyphenyl)-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)-(CA INDEX NAME)

Absolute stereochemistry.

RN 871713-85-8 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

RN 871713-88-1 CAPLUS

CN 2H-Isoindole-2-butanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]-1,3-dihydro- $\alpha$ , $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-89-2 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-90-5 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]-  $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-2-(2-thiazolyl)-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

RN 871713-91-6 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]-2-(4-fluorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-92-7 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[[5-(2-ethoxyphenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-93-8 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-[2-(1-methylethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

RN 871713-94-9 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[[5-[2-(phenylmethoxy)phenyl]-2-pyridinyl]methyl]-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-95-0 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-cyanophenyl)-2-pyridinyl]methyl]-  $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871713-96-1 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-(2-methoxyphenyl)-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)-(CA INDEX NAME)

RN 871723-96-5 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[1-[5-(2-cyanophenyl)-2-pyridinyl]ethyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871723-99-8 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[1-[5-[2-(aminocarbonyl)phenyl]-2-pyridinyl]ethyl]-2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871724-02-6 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[1-[5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]ethyl]-, ( $\alpha$ R,  $\beta$ R, 2R)- (CA INDEX NAME)

RN 871724-05-9 CAPLUS

CN 1-Pyrrolidinebutanamide, 2-(3-chlorophenyl)-N-[1-[5-(2-ethoxyphenyl)-2-pyridinyl]ethyl]- $\alpha$ , $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-75-5 CAPLUS

CN 2H-Isoindole-2-butanamide, N-[[6-cyano-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]-1,3-dihydro- $\alpha$ , $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-76-6 CAPLUS

CN 1-Pyrrolidinebutanamide,  $\alpha$ ,  $\beta$ -dihydroxy-N-[[6-methoxy-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

RN 871728-77-7 CAPLUS

CN 1-Pyrrolidinebutanamide,  $\alpha$ ,  $\beta$ -dihydroxy-N-[[1-oxido-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-78-8 CAPLUS

CN 2H-Isoindole-2-butanamide, 1,3-dihydro- $\alpha$ , $\beta$ -dihydroxy-N-[[1-oxido-5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]- $\gamma$ -oxo-, ( $\alpha$ R, $\beta$ R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 871728-79-9 CAPLUS

CN 1-Pyrrolidinebutanamide, N-[[5-(2-ethoxy-4-fluorophenyl)-2-pyridinyl]methyl]- $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-, ( $\alpha$ R,  $\beta$ R)- (CA INDEX NAME)

RN 871728-80-2 CAPLUS

CN 1-Pyrrolidinebutanamide,  $\alpha$ ,  $\beta$ -dihydroxy- $\gamma$ -oxo-N-[[5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]-,  $(\alpha R, \beta R)$ - (CA INDEX NAME)

Absolute stereochemistry.

RN 871729-25-8 CAPLUS

CN 2-Pyridinepropanamide,  $\alpha$ ,  $\beta$ -dihydroxy-N-[[5-[2-(trifluoromethoxy)phenyl]-2-pyridinyl]methyl]-, ( $\alpha$ R,  $\beta$ S)- (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:612238 CAPLUS

DOCUMENT NUMBER: 143:133188

TITLE: Preparation of  $\alpha$ -hydroxy carboxamides,

particularly N-biphenylmethyl and

N-phenylpyridin-2-ylmethyl amides, as bradykinin B1

antagonists or inverse agonists useful in the treatment of pain and inflammation INVENTOR(S): Wood, Michael R.; Anthony, Neville J.; Bock, Mark G.; Kuduk, Scott D. PATENT ASSIGNEE(S): Merck & Co., Inc., USA SOURCE: PCT Int. Appl., 51 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION: APPLICATION NO. PATENT NO. KIND DATE \_\_\_\_ \_\_\_\_\_\_ \_\_\_\_\_ 20050714 WO 2004-US42691 WO 2005063690 A1 20041217 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG MR, NE, SN, TD, TG AU 2004-309357 A1 AU 2004309357 20050714 20041217 CA 2550372 Α1 20050714 CA 2004-2550372 20041217 CA 2550372 С 20090929 20061004 EP 2004-814829 EP 1706372 A120041217 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS CN 1898198 A 20070117 CN 2004-80038255 20041217 BR 2004017928 Α 20070417 BR 2004-17928 20041217 JP 2007520472  $\mathbf{T}$ 20070726 JP 2006-547200 20041217 ZA 2006004398 A 20071227
IN 2006DN03156 A 20070824
US 20080318976 A1 20081225
MX 2006007203 A 20060818
KR 2006115753 A 20061109
NO 2006003394 A 20060912 ZA 2006-4398 20060530 IN 2006-DN3156 20060602 US 2006-583675 20060619 MX 2006-7203 20060621 KR 2006-712382 20060621 KR 2006-712382 20060621 NO 2006-3394 20060721 US 2003-531643P P 20031222 US 2004-539637P P 20040128 NO 2006003394 PRIORITY APPLN. INFO.: P 20041104 US 2004-624958P WO 2004-US42691 W 20041217

OTHER SOURCE(S): CASREACT 143:133188; MARPAT 143:133188

GΙ

AB Title compds. [I; Y = CH, N; R1 = (un)substituted Ph, 2,2-dioxo-2,1-benzisothiazolin-1-yl; R2 = H, (un)substituted alkyl, Ph, etc.; R3 = defined as R2; or R3 = OH; or R2CR3 = (un)substituted 3-7-membered carbocyclyl; R4, R5 = independently H, halo/alkyl; R7 = H, halo] were prepared as bradykinin B1 antagonists or inverse agonists useful in the treatment of pain and inflammation associated with the bradykinin B1 pathway. For example, coupling of 1-hydroxycyclopropanecarboxylic acid with Me 4'-(aminomethyl)biphenyl-2-carboxylate gave amide II. I have affinity for the B1 receptor in a radioligand assay as demonstrated by results of less than 5  $\mu$ M [sic].

IT 858412-39-2P, (2R)-N-[(1R)-1-[5-[5-Chloro-3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-3-fluoropyridin-2-yl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methylpropanamide 858412-96-1P

858412-97-2P 858412-98-3P 858412-99-4P 858413-00-0P 858413-01-1P 858413-05-5P 858413-08-8P 858413-13-5P 858413-14-6P 858413-15-7P 858413-16-8P 858413-22-6P 858413-23-7P 858413-25-9P 858413-24-8P 858413-26-0P 858413-32-8P 858413-33-9P 858413-34-0P 858413-35-1P 858413-36-2P 858413-37-3P 858413-38-4P 858413-39-5P 858413-40-8P 858413-41-9P 858413-43-1P 858413-45-3P 858413-46-4P 858413-47-5P 858413-48-6P 858413-49-7P 858413-50-0P 858413-52-2P 858413-53**-**3P 858413-54**-**4P 858413-56-6P 858413-57-7P 858413-59-9P 858413-60-2P 858413-61-3P 858413-62-4P 858413-63-5P 858413-64-6P 858413-68-0P 858413-69-1P 858413-70-4P 858413-72-6P 858413-73-7P 858413-78-2P 858413-79-3P 858413-80-6P 858413-81-7P 858413-82-8P 858413-85-1P 858413-86-2P 858413-92-0P 858413-95-3P 858413-96-4P 858413-94-2P 858413-98-6P 858413-99-7P 858414-00-3P 858414-01-4P 858414-02-5P 858414-03-6P 858414-04-7P 858414-06-9P 858414-07-0P 858414-08-1P 858414-09-2P 858414-10-5P 858414-11-6P 858414-13-8P 858414-12-7P 858414-14-9P 858414-15-0P 858414-16-1P 858414-17-2P 858414-18-3P 858414-27-4P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of N-biphenylmethyl and N-phenylpyridin-2-ylmethyl  $\alpha$ -hydroxycarboxamides as bradykinin Bl antagonists or inverse agonists useful in the treatment of pain and inflammation)

RN 858412-39-2 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[5-chloro-3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 858412-96-1 CAPLUS

CN Benzoic acid, 4-chloro-2-fluoro-6-[5-fluoro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.

RN 858412-97-2 CAPLUS

CN Propanamide, 3,3,3-trifluoro-N-[(1R)-1-[3-fluoro-5-[3-fluoro-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-2-pyridinyl]ethyl]-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

RN 858412-98-3 CAPLUS

CN Benzoic acid, 4-chloro-2-fluoro-6-[5-fluoro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.

RN 858412-99-4 CAPLUS

CN Benzoic acid, 2,4-dichloro-6-[5-fluoro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, methyl ester (CA INDEX NAME)

RN 858413-00-0 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3,5-dichloro-2-(2,2-difluoroethoxy)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-01-1 CAPLUS

CN Propanamide, N-[(1R)-1-[5-(3,5-dichloro-2-ethoxyphenyl)-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

858413-05-5 CAPLUS Propanamide, N-[(1R)-1-[5-(3,5-dichloro-2-cyanophenyl)-3-fluoro-2-CN pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-08-8 CAPLUS RN

Propanamide, N-[(1R)-1-[5-[5-chloro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-2-(2,2,2-fluoro-3-fluoro-2-(2,2,2-fluoro-2-(2,2CN trifluoroethoxy)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

858413-13-5 CAPLUS Propanamide, N-[(1R)-1-[3-chloro-5-[3,5-dichloro-2-(2,2,2-CN trifluoroethoxy)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-14-6 CAPLUS RN

Propanamide, N-[(1R)-1-[3-chloro-5-[3-fluoro-2-(2-methyl-2H-tetrazol-5-1]]CN yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

858413-15-7 CAPLUS Propanamide, N-[(1R)-1-[5-[3,5-dichloro-2-(1-methylethoxy)phenyl]-3-fluoro-CN 2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-16-8 CAPLUS RN

Propanamide, N-[(1R)-1-[5-[3,5-dichloro-2-(2-methyl-2H-tetrazol-5-methCN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R) - (CA INDEX NAME)

RN 858413-22-6 CAPLUS

CN Benzamide, 2,4-dichloro-6-[5-fluoro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]- (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-23-7 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3-chloro-2-(ethylthio)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

RN 858413-24-8 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3,5-dichloro-2-(2,2,2-trifluoroethoxy)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-25-9 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3,5-dichloro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

RN 858413-26-0 CAPLUS

CN Benzoic acid, 2-[5-chloro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-6-fluoro-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-32-8 CAPLUS

CN Propanamide, N-[(1R)-1-[3-chloro-5-[3-chloro-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

858413-33-9 CAPLUS Propanamide, N-[(1R)-1-[5-[5-chloro-2-(2,2-difluoroethoxy)-3-fluorophenyl]-CN 3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858413-34-0 CAPLUS RN

Benzoic acid, 2,4-dichloro-6-[5-chloro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-CN hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, methyl ester (CA INDEX NAME)

RN 858413-35-1 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3,5-dichloro-2-(2-methylpropoxy)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-36-2 CAPLUS

CN Benzoic acid, 2-chloro-6-[5-fluoro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, ethyl ester (CA INDEX NAME)

RN 858413-37-3 CAPLUS

CN Benzoic acid, 2,4-dichloro-6-[5-fluoro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-38-4 CAPLUS

CN Benzoic acid, 2-chloro-6-[5-fluoro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, methyl ester (CA INDEX NAME)

RN 858413-39-5 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3-chloro-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-40-8 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3-chloro-2-(ethylsulfinyl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

RN 858413-41-9 CAPLUS

CN Benzoic acid, 2-chloro-6-[5-chloro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-43-1 CAPLUS

CN Propanamide, 3,3,3-trifluoro-N-[(1R)-1-[3-fluoro-5-[3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-2-pyridinyl]ethyl]-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

858413-45-3 CAPLUS Propanamide, N-[(1R)-1-[3-chloro-5-[3,5-dichloro-2-(2-methyl-2H-tetrazol-5-CN y1)pheny1]-2-pyridiny1]ethy1]-3,3,3-trifluoro-2-hydroxy-2-methy1-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858413-46-4 CAPLUS RN

CN Propanamide, N-[(1R)-1-[3-chloro-5-[3,5-dichloro-2-(5-methyl-1,2,4-methyl-1,4-methyl-1oxadiazol-3-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2methyl-, (2R)- (CA INDEX NAME)

858413-47-5 CAPLUS Propanamide, N-[(1R)-1-[5-[5-chloro-3-fluoro-2-(2-methyl-2H-tetrazol-5-CN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-48-6 CAPLUS RN

CNPropanamide, 3,3,3-trifluoro-N-[(1R)-1-[3-fluoro-5-[3-fluoro-2-(3-methyl-special points)])1, 2, 4-oxadiazol-5-yl) phenyl]-2-pyridinyl]ethyl]-2-hydroxy-2-methyl-, ( $\overline{2}R$ )-(CA INDEX NAME)

858413-49-7 CAPLUS Propanamide, N-[(1R)-1-[5-[3-chloro-2-(5-methyl-1,2,4-oxadiazol-3-  $^{\circ}$ CN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-50-0 CAPLUS RN

CN Propanamide, N-[(1R)-1-[5-[5-chloro-3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R) - (CA INDEX NAME)

858413-52-2 CAPLUS Propanamide, N-[(1R)-1-[3-chloro-5-[3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-CN yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858413-53-3 CAPLUS RN

CN Propanamide, N-[(1R)-1-[3-chloro-5-[5-chloro-3-fluoro-2-(3-methyl-1,2,4-methyl-1,4-metoxadiazol-5-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2methyl-, (2R)- (CA INDEX NAME)

 $858413-54-4 \quad \text{CAPLUS} \\ \text{Propanamide, N-[(1R)-1-[3-chloro-5-[3-chloro-2-(5-methyl-1,2,4-oxadiazol-3-methyl-3-me$ CN yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858413-56-6 CAPLUS RN

CN Propanamide, N-[(1R)-1-[3-chloro-5-[3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-methyl-3-methylyl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

858413-57-7 CAPLUS Propanamide, N-[(1R)-1-[3-chloro-5-[5-chloro-3-fluoro-2-(2-methyl-2H-  $^{\circ}$ CN tetrazol-5-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-59-9 CAPLUS RN

Propanamide, N-[(1R)-1-[5-[3-chloro-2-(3-methyl-1,2,4-oxadiazol-5-CN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R) - (CA INDEX NAME)

858413-60-2 CAPLUS Propanamide, N-[(1R)-1-[5-[3-chloro-5-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-fluoro-3 CN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-61-3 CAPLUS

Propanamide, N-[(1R)-1-[5-[3-chloro-5-fluoro-2-(2-methyl-2H-tetrazol-2-(2-methyl-2H-tetrazol-2-(2-methyl-2H-tetrazol-2-(2-methyl-2H-tetrazol-2-(2-methyl-2H-tetrazol-2-(2-methyl-2H-tetrazol-2-(2-methyl-2H-tetrazol-2-(2-methyl-2-(2CNyl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R) - (CA INDEX NAME)

RN 858413-62-4 CAPLUS

CN Benzoic acid, 2,4-dichloro-6-[5-chloro-6-[(1R)-1-[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-63-5 CAPLUS

CN Propanamide, N-[(1R)-1-[3-chloro-5-[5-chloro-3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

858413-64-6 CAPLUS Propanamide, N-[(1R)-1-[5-[3,5-dichloro-2-(3-methyl-1,2,4-oxadiazol-5-CN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-68-0 CAPLUS RN

Propanamide, N-[(1R)-1-[5-[3,5-difluoro-2-(3-methyl-1,2,4-oxadiazol-5-CN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R) - (CA INDEX NAME)

858413-69-1 CAPLUS Propanamide, N-[(1R)-1-[5-[3,5-difluoro-2-(2-methyl-2H-tetrazol-5-CN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-70-4 CAPLUS RN

CN Benzoic acid, 2,4-dichloro-6-[6-[(1R)-1-[(2R)-3,3,3-trifluoro-2-hydroxy-2methyl-1-oxopropyl]amino]ethyl]-3-pyridinyl]-, methyl ester (CA INDEX NAME)

RN 858413-72-6 CAPLUS

CN Propanamide, N-[(1R)-1-[3-chloro-5-[3-chloro-5-methyl-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-73-7 CAPLUS

CN Propanamide, N-[(1R)-1-[3-chloro-5-[3-chloro-5-methyl-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

858413-78-2 CAPLUS Propanamide, N-[(1R)-1-[5-[3,5-difluoro-2-(5-methyl-1,2,4-oxadiazol-3-  $^{\circ}$ CN yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-79-3 CAPLUS RN

CN Propanamide, N-[(1R)-1-[3-chloro-5-[3,5-difluoro-2-(5-methyl-1,2,4-methyl-1,4-methyl-1oxadiazol-3-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2methyl-, (2R)- (CA INDEX NAME)

858413-80-6 CAPLUS Propanamide, N-[(1R)-1-[3-chloro-5-[3,5-difluoro-2-(2-methyl-2H-tetrazol-5-CN yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858413-81-7 CAPLUS RN

CNPropanamide, N-[(1R)-1-[5-[3-chloro-2-(ethylsulfonyl)phenyl]-3-fluoro-2pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

RN 858413-82-8 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3,5-dichloro-2-[5-(1-methylethyl)-1,2,4-oxadiazol-3-yl]phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-85-1 CAPLUS

CN Propanamide, N-[(1R)-1-[5-[3-chloro-5-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]-3-fluoro-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

858413-86-2 CAPLUS Propanamide, N-[(1R)-1-[3-chloro-5-[3,5-difluoro-2-(3-methyl-1,2,4-CN oxadiazol-5-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858413-92-0 CAPLUS RN

CN Benzoic acid, 2-[5-chloro-6-[[[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1oxopropyl]amino]methyl]-3-pyridinyl]-6-fluoro-, methyl ester (CA INDEX NAME)

RN 858413-94-2 CAPLUS

CN Propanamide, N-[[5-[3,5-dichloro-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-3-fluoro-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 858413-95-3 CAPLUS

CN Propanamide, N-[[5-[5-chloro-3-fluoro-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-3-fluoro-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

 $858413-96-4 \quad \text{CAPLUS} \\ \text{Propanamide, N-[[3-chloro-5-[5-chloro-3-fluoro-2-(2-methyl-2H-tetrazol-5-methyl-2H-t$ CN yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858413-98-6 CAPLUS RN

CN Propanamide, N-[[3-chloro-5-[5-chloro-3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R) - (CA INDEX NAME)

CN y1)pheny1]-2-pyridiny1]methy1]-3,3,3-trifluoro-2-hydroxy-2-methy1-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858414-00-3 CAPLUS RN

Propanamide, N-[[3-chloro-5-[5-chloro-3-fluoro-2-(3-methyl-1,2,4-oxadiazol-CN 5-yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R) - (CA INDEX NAME)

 $858414-01-4 \quad \text{CAPLUS} \\ \text{Propanamide, N-[[3-chloro-5-[3-fluoro-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-} \\ \\ \text{Propanamide, N-[[3-chlor$ CN 2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858414-02-5 CAPLUS RN

CN Propanamide, N-[[5-[3,5-difluoro-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-3fluoro-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

858414-03-6 CAPLUS Propanamide, N-[[5-[5-chloro-3-fluoro-2-(5-methyl-1,2,4-oxadiazol-3-CN yl)phenyl]-3-fluoro-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858414-04-7 CAPLUS RN

CN Propanamide, 3,3,3-trifluoro-N-[[3-fluoro-5-[3-fluoro-2-(2-methyl-2Htetrazol-5-yl)phenyl]-2-pyridinyl]methyl]-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

858414-06-9 CAPLUS Propanamide, N-[[3-chloro-5-[3,5-difluoro-2-(2-methyl-2H-tetrazol-5-CN yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858414-07-0 CAPLUS RN

CN Propanamide, N-[[3-chloro-5-[3-chloro-2-(2-methyl-2H-tetrazol-5-yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

858414-08-1 CAPLUS Propanamide, N-[[3-chloro-5-[3,5-dichloro-2-(3-methyl-1,2,4-oxadiazol-5-CN y1)pheny1]-2-pyridiny1]methy1]-3,3,3-trifluoro-2-hydroxy-2-methy1-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858414-09-2 CAPLUS RN

CN Propanamide, N-[[3-chloro-5-[3,5-difluoro-2-(5-methyl-1,2,4-oxadiazol-3-methyl-3yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

858414-10-5 CAPLUS Propanamide, N-[[3-chloro-5-[3,5-difluoro-2-(3-methyl-1,2,4-oxadiazol-5-CN yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858414-11-6 CAPLUS RN

CN Propanamide, N-[[3-chloro-5-[3-chloro-5-fluoro-2-(2-methyl-2H-tetrazol-5yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

858414-12-7 CAPLUS Propanamide, N-[[3-chloro-5-[3-chloro-5-fluoro-2-(3-methyl-1,2,4-oxadiazol-CN 5-yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858414-13-8 CAPLUS RN

CN Benzoic acid, 4-chloro-2-[5-chloro-6-[[[(2R)-3,3,3-trifluoro-2-hydroxy-2methyl-1-oxopropyl]amino]methyl]-3-pyridinyl]-6-fluoro-, methyl ester (CA INDEX NAME)

RN 858414-14-9 CAPLUS

CN Propanamide, N-[[3-chloro-5-[3,5-dichloro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

RN 858414-15-0 CAPLUS

CN Propanamide, N-[[5-[3,5-dichloro-2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-3-fluoro-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

858414-16-1 CAPLUS Propanamide, N-[[3-chloro-5-[3-chloro-2-(3-methyl-1,2,4-oxadiazol-5-CN yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)-(CA INDEX NAME)

Absolute stereochemistry.

858414-17-2 CAPLUS RN

Propanamide, N-[[3-chloro-5-[3-chloro-5-fluoro-2-(5-methyl-1,2,4-oxadiazol-CN 3-yl)phenyl]-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R) - (CA INDEX NAME)

858414-18-3 CAPLUS Propanamide, N-[[5-[5-chloro-3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-CN yl)phenyl]-3-fluoro-2-pyridinyl]methyl]-3,3,3-trifluoro-2-hydroxy-2-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

858414-27-4 CAPLUS RN

CN Propanamide, N-[(1R)-1-[3-chloro-5-[3,5-dichloro-2-(3-methyl-1,2,4-methyl-1,4-methyl-1oxadiazol-5-yl)phenyl]-2-pyridinyl]ethyl]-3,3,3-trifluoro-2-hydroxy-2methyl-, (2R)- (CA INDEX NAME)

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